

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	D. Tracy	Group Art Unit:	2857
Serial Number:	10/556,306	Examiner:	F. E. Suarez
Filing Date:	January 27, 2006	Docket No.:	B 545
Title:	Method and Apparatus for Quantitating Surface-Binding Optical Resonance Profiles		

Commissioner for Patents
P.O. Box 1450
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**Declaration of Prior Invention in the United States
or in a NAFTA or WTO Country
to Overcome Cited Patent or Publication (37 C.F.R. § 131)**

1. This declaration is to establish completion of the invention in this application in the United States, as a date prior to April 10, 2003. The effective date of the United States Patent No. 6,819,812 (Kochergin et al.) was April 14, 2003. The earliest possible effective date of the United States Patent No. 7,283,242 (Thornton) was April 11, 2003.
2. The person making this declaration is the inventor.
3. To establish the date of completion of the invention of this application, a copy of the initial invention disclosure in the form of an internal technical memorandum by the inventor is submitted as evidence; the date has been obliterated. This document (HTS

BioSystems Technical Memorandum, Re: EPF Profile Fit Software Design Proposal), has a date prior to April 10, 2003, thus, invention claimed in this application was made prior to April 10, 2003, which is a date earlier than the effective date of each of the references.

4. From the accompanying document, it is clear that the inventor had constructive reduction to practice of the invention in this application before April 10, 2003.
5. This declaration is submitted after final rejection.

As a person signing below:

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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HTS BioSystems Technical Memorandum

To: Keith Ferrara, Robert Kersten, David Verbarq, Mike Reiman
CC: Paul Hetherington, Enrico Picozza
From: David H. Tracy
Date: [REDACTED]
Re: **EPF Profile Fit Software Design Proposal**

Background

Empirical Profile Fits (EPF) have been shown to work at least as well as polynomial fits in quantitating SPR resonances, and may work slightly better. Shot noise limited performance is a few 10's of microdegrees. EPF's have the advantage of allowing much sparser angular point spacing, which can increase scan speed several-fold. This is especially true when long scans are needed to accommodate a wide range of SPR shifts in certain experiments.

The current implementation, in *FitSPR.xls*, is jury rigged and rather crude. It also lacks certain features needed for incorporation into instrument software, such as adequate error handling and fully automatic determination of fitting windows. It is planned to rewrite much of it in order to make it simpler and more robust. The existing Excel VBA shell will still be used to exercise and test it. The core VBA objects can then be compiled into .ocx or .dll files for incorporation into instrument software.

Although we can remain quite flexible, and changes can be incorporated quickly, the following outline design is suggested for consideration. It will save time and trouble if basic architectural issues are identified and resolved up front, so please bring any concerns/comments to my attention as soon as possible.

Block Diagram

The process involved in EPF peak finding naturally divides into two parts, which can be identified with two separate objects in software. These are the Calibration stage and the Fit stage.

In the Calibration stage, SPR data are obtained under fixed conditions over a relatively long angle range, with relatively small angle steps. The precise values of these parameters need not be fixed, and can be varied as experience demands, but 0.05 deg steps, as currently employed, are probably suitable. These steps will be referred to as **Base Steps** and are indexed by **Base Index** values. The raw scans so obtained, one for each ROI being calibrated, are (optionally) smoothed and then subsampled to increase the point density by 2^N , where $N=1$ to 5. Lagrange interpolation (4 or 6 point) is used to implement the subsampling. Derivatives of the subsampled profiles are then computed using Savitsky Golay filters. Certain properties of the profiles are calculated, such as approximate resonance position, depth and width, in order to qualify the

resonances as adequate and correct. These results are then stored in preparation for later fitting procedures.

In the Fitting stage, angle scans are measured for particular ROI's during an experiment. These scans may be obtained at much lower point density than that of the Calibration scans, and possibly over shorter angle ranges. However, *each angle position used must be one of those used in the calibration stage* and is referred to by its Base Index value. The role of the Fitting module is to look at these experimental scans, identify the region encompassing the resonance, and fit that region using empirical profiles stored above in order to quantify the shift in the resonance **as compared to its angular location at Calibration time**. Absolute angular positions cannot be measured accurately, although rough values can be obtained by adding the shifts to the nominal peak location determined during calibration.

A block diagram of the whole business is shown below.

Exposed Methods for Calibration

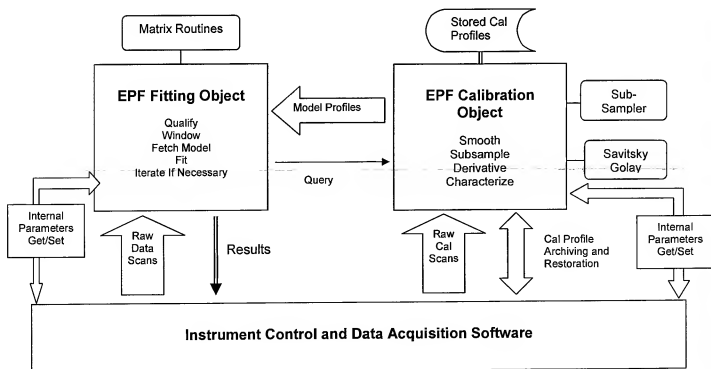
Each method is a Boolean Function returning True on failure.

C_epfCalib_Calculate (ChipID, ROI_list(i), CalScanArray(i,j))

ChipID is a structure identifying the device being calibrated, when, under what conditions, etc.

ROI_list(i) is a vector of identifiers (variants) for the ROI's being calibrated.

CalScanArray(i,j) is a 2-D array of scans, one for each ROI, indexed by i. The angle step index j (Base Index) is very important. Values of j must be integers with unit steps, but may start and end at any values (j0,j1). These base index values must be remembered, as later data scan angles will be identified with these same base indices.



C_epfCalib_Erase

Erase internally stored EPF profiles and derivatives to recover memory and prevent accidental use of incorrect calibrations.

C_epfCalib_Extract (*ChipID*, *ROI_List(i)*, *ProfileProperties(i)*, *nSubSample*,
SubSampledProfiles(i,k))

Note: Output parameters are indicated by *italics*, input by normal font.

ProfileProperties(i) is a vector of profile specific structures, each of which contains:

Nominal_Resonance_Location in Base Index terms (double) *

Nominal FWHM of Resonance (double) in BaseSteps *

Nominal Fractional Depth of Resonance (double) *

Max Intensity of Profile (double) *

Quality of Profile & Calibration (Integer) (OK, Poor, Bad)

Reason-not-OK (string)

* These results are checked against tolerance limits by the program and exceptions reported back under Quality of Result.

NSubSample (Integer) The subsampling factor employed to generate the profiles (as was specified in internal control parameter set)

SubSampledProfiles(i,k) The finished profiles used for fitting, indexed by the ROI index *i* and the subsampled angle step index *k*. Each step in *j* corresponds to *nSubSample* steps in *k*.

All of this data must be archived (stored to disc, e.g.) in order to restore the calibration later without re-running it. One might choose to run the calibration once, for example, when a new chip is first put into service. Then, for each subsequent session, the same stored calibration could be restored. Derivatives are not extracted or restored; instead, they are recalculated as necessary upon restoration.

C_epfCalib_Restore (*ChipID*, *ROI_List(i)*, *ProfileProperties(i)*, *nSubSample*,
SubSampledProfiles(i,k))

Restore the calibration. It is possible to edit some of these data before restoration -- for example, ROI names could be changed or certain ROI's deleted from the set.

Exposed Method for Fitting

Only one ROI is fitted per call. This allows flexibility, in that other work can be done in between ROI fits, such as plotting results incrementally. Also, this allows more detailed error and problem reporting on a per ROI rather than global basis. Fitting is more complex and tricky than Calibration, but there is only one basic method involved.

C_epfFit_FitSPR (ChipID, ROI_label_of_Calibration_to_Use, BaseIndex0, BaseIndexStep, ScanData(p), Results)

Boolean, returning True if any trouble was encountered. This may not necessarily mean result is useless. See Results for details.

ROI_Label_of_Calibration_to_Use (variant) The label for the ROI whose EPF calibration profiles are to be used for the fit. Need not be the actual ROI being measured, but normally will be. Must be one of the set in the ROI_List used in the Calibration stage.

BaseIndex0 (Integer) The BaseIndex of the angle of the first element in the ScanData array.

BaseIndexStep (Integer) The increment in Base Index between successive angle steps in the ScanData vector. Must be positive, typically 1 - 6 or so.

ScanData(p) (Double array) Signals at each of several angles indexed by p. The actual Base Indices are as given by BaseIndex0 and BaseIndexStep. Index p is a dummy index, and may start at any convenient value.

Results (structure). Contains the following:

Shift (double) shift relative to epf model in units of base steps **[This is the main answer]**

Fitted Location (double) Nominal location of epf model profile + Shift above

RMS Residual of Fit (double) can be used to judge accuracy and detect misshapen profiles. Also helps detect gross fitting errors due to totally wrong position determination.*

Amplitude of fit (double) Use to detect major errors. Should be close to unity, unless something caused a drastic change in signal intensity.*

BaseLine of Fit (double) Represents change in apparent baseline offset (in counts) since the calibration run. May be of either sign, but should be small.*

Quality of Result (integer) OK, Marginal, Bad. Marginal may indicate useful result, but with reduced precision.

ReasonWhyBad (string) Explanation of problem, if any

- These results are checked against tolerance limits by the program and exceptions reported back under Quality of Result.

Note: A second similar method to **C_epfFit_FitSPR** may be included which returns more detailed diagnostic data, such as actual fit and residual vectors suitable for graphing. This could be very useful for troubleshooting.